

**13. Diseases of the Musculoskeletal System and Connective Tissue****Reference**

Ohta H, Nemoto K. Combined effect of vitamin D<sub>3</sub> and TSUMURA Keishibukuryogan on osteopenia following oophorectomy\*. *Kampo Igaku (Science of Kampo Medicine)* 1989; 13: 173–9 (in Japanese).

**1. Objectives**

To evaluate the combined effect of keishibukuryogan (桂枝茯苓丸) and vitamin D<sub>3</sub> on osteopenia in women during menopause.

**2. Design**

Randomized controlled trial (RCT).

**3. Setting**

One facility (Department of Obstetrics and Gynecology, Tokyo Electric Power Hospital), Japan.

**4. Participants**

Thirty patients diagnosed with osteopenia following oophorectomy at the above facility, with a total bone mineral density (MD) score of 4 or more points.

**5. Intervention**

Arm 1: oral TSUMURA Keishibukuryogan (桂枝茯苓丸) Extract Granules 2.5 g t.i.d. before meals +  $\alpha$ -calcidol 0.5  $\mu$ g b.i.d. after meals (n=6).

Arm 2: oral  $\alpha$ -calcidol 0.5  $\mu$ g b.i.d. after meals (n=6).

Arm 3: oral  $\alpha$ -calcidol 0.5  $\mu$ g b.i.d. after meals + Premarin 0.625 mg q.d. after meals or Metharmon F tablet t.i.d. after meals (n=7).

Arm 4: follow-up without drug administration (n=11).

**6. Main outcome measures**

Change in MD (mean percentage change in actual values of 5 variables: bone cortex width index, bone marrow width, bone cortex and marrow integrated density index, bone cortex density index, and bone density per unit length) compared between baseline and after 10 months of treatment.

Serum concentration of bone metabolic markers (alkaline phosphatase [AL-P], calcium [Ca], and phosphate [P] compared between baseline and after 10 months of treatment).

**7. Main results**

Combination of keishibukuryogan and vitamin D<sub>3</sub> significantly increased bone mineral content compared with baseline ( $P<0.05$ ), vitamin D<sub>3</sub> alone, and no drug administration ( $P<0.05$ ) and significantly increased serum AL-P and Ca concentrations ( $P<0.05$ ). The hormones increased serum Ca concentration ( $P<0.05$ ).

**8. Conclusions**

Combination of keishibukuryogan and vitamin D<sub>3</sub> decreased osteopenia in women without ovaries.

**9. From Kampo medicine perspective**

Keishibukuryogan controlled mental and physical disorders associated with ovarian deficiency syndrome consisting of *qi-no-josho* (気の上衝, *qi* counterflow pattern syndrome), *oketsu* (才血, blood stasis), and *suidoku* (水毒, water toxin), resulting in increases in appetite, and consequently Ca intake, intestinal absorption and motility, which may have indirectly increased bone mineral content.

**10. Safety assessment in the article**

Not mentioned.

**11. Abstractor's comments**

A representative *kuoketsuzai* (驅才血劑, blood stasis-expelling formula), keishibukuryogan improves *suidoku* and *qitai* (気滯, *qi* stagnation) and is therefore frequently used for treatment of unidentified complaints in postmenopausal women. This study demonstrated that use of vitamin D<sub>3</sub> as an adjuvant increases bone mineral content in patients following ovariectomy. Given that long-term intervention is needed to prevent and treat osteoporosis, a Kampo therapy such as keishibukuryogan can be optimal. However, the need for keishibukuryogan in therapy according to *sho* (証, pattern) of postmenopausal women with unidentified complaints, most whom have *kyosho* (虚証, deficiency pattern), should be investigated.

**12. Abstractor and date**

Ushiroyama T, 16 August 2008, 1 June 2010, 31 December 2013.